REMARKS

I. STATUS OF THE CLAIMS

Claims 1 to 7 have been considered by the Examiner, while claims 8 to 10 and 12 have been withdrawn.

Claims 1, 3, and 4-7 have been amended. These amendments find support in original claims 1, 4, and 5 as originally filed, and in the specification on page 14, third paragraph to page 15, first paragraph and on page 16, first to fourth paragraph of the description of the present patent application as originally filed. No new matter has been added.

Claims 14 and 15 are new. Support for these claims can be found in original claims 4 and 6. No new matter has been added.

Claims 11 and 13 have been cancelled.

II. Response to Claim Objections

The Examiner notes that the abbreviations E2F, E1A, and E1B should be spelled out at the first encounter in the claims.

Claim 1 has been amended to refer to "an early region 1A (E1A) gene" and the second viral gene codes for an "early region 1B 55K (E1B 55K)" protein. Thus, the objection regarding the abbreviations E1A and E1B has been addressed.

As to the abbreviation E2F, Applicants respectfully note that "E2F" is not an abbreviation. The designation "E2F transcription factor" is the only known

designation present in the art. *See e.g.* Kim et al. (1995, Oncogene 20: 2671-2682). Thus, the objection should be withdrawn, as the claim recites the full term for the protein of interest.

The Examiner objects to the word "brain" in claim 3. The term "brain" is no longer part of amended claim 3. Accordingly, this objection no longer applies.

Applicants respectfully request that the claim objections be withdrawn.

III. RESPONSE TO REJECTIONS UNDER 35 USC § 112 – SECOND PARAGRAPH

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully disagree with this rejection, but have amended the claims to expedite prosecution.

The Examiner states that the term "and/or" in claim 1 renders said claim unclear. Claim 1 as amended no longer contains the term "and/or", and thus this rejection does no longer apply.

The Examiner alleges that the term "derived from" in claims 3 and 4 renders said claims unclear. While Applicants disagree with the rejection, in order to expedite prosecution, the term "derived from" has been replaced with the term "obtained from", as suggested by the Examiner.

The Examiner notes that the use of parenthesis in claims 3 and 4 renders said claims unclear. The parentheses in claim 3 and 4 have been removed, thus obviating this rejection.

The Examiner also rejects claim 4 due to use of "or" and "and", rather than Markush group format. Applicants disagree with this rejection. However, claim 4 has been amended to reword the allegedly confusing use of these terms. Claims

3 and 5 have also been amended accordingly to remove this allegedly confusing wording.

Applicants assert that the claims as amended satisfy all of the requirements of 35 USC § 112, and respectfully ask that the rejection be withdrawn.

IV. RESPONSE TO REJECTIONS UNDER 35 USC § 112 – DEPOSIT REQUIREMENT

The Examiner asserts that claims 1 and 7 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner asserts that specification lacks complete deposit information for the deposit of cell line 12A07-A10 (DSM ACC2695) deposited on Oct. 20, 2004.

Applicants have included the document "Declaration Regarding 12A07-A10 (DSM-ACC2695) Cell Line Deposit Under 27 C.F.R. §1.808" along with this response, which includes a Deposit Receipt and Viability Report of deposited cell line 12A07-A10 (DSM-ACC2695). Applicants assert that all of the requirements to satisfy enablement by deposit of biological material (37 C.F.R. § 1.801-1.809) been fulfilled, and the rejection should be withdrawn.

V. RESPONSE TO REJECTIONS UNDER 35 USC § 102

The Action rejects claim 1 under 35 U.S.C. § 102(b) as being anticipated by Kim et al. (1995, Oncogene 20: 2671-2682)(hereafter "Kim"). Applicants respectfully disagree with this rejection.

As an initial matter, claim 1 has been amended to refer to "an immortalized avian cell line which comprises a combination of viral genes", comprising E1A and E1B.

Amended claim 1 and dependent claims 2 to 7 are not anticipated by the teachings of Kim, for the cell lines disclosed in Kim do not contain viral genes. Kim discloses immortalized chicken embryo fibroblast (CEF) cells which were non-virally and non-chemically immortalized and established in continuous cell culture (see abstract and "materials and methods", paragraph "cells and culture conditions" on page 2680, left column of Kim). Thus, Kim does not anticipate claims 1-7 because it does not disclose "an immortalized avian cell line which comprises a combination of viral genes."

Indeed, the Action recognizes this distinction, noting that Kim discloses a "number of **non-virally** and non-chemically immortalized chicken cell lines characterized by diminished steady-state expression of p53 mRNA with dramatically elevated E2F-1 mRNA levels". (emphasis added)(Action, at p.10). As recognized by the Examiner, Kim does not disclose virally immortalized cells.

Finally, no specific viral genes are discussed in Kim, such as E1A and E1B 55K protein from mastadenoviruses. Since the avian cells claimed comprise viral genes, Kim cannot anticipate the cells recited in claim 1.

Kim does not disclose the immortalized avian cell line as claimed. Accordingly, the avian cell line according to amended claim 1 is not anticipated by Kim. Since claims 2 to 7 by are dependent directly or indirectly on amended claim 1, these claims incorporate the same features of claim 1 and are also therefore not anticipated by Kim. Applicants respectfully request reconsideration of this rejection.

VI. RESPONSE TO REJECTIONS UNDER 35 USC § 103

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bouquet et al., (U.S. Patent 6,255,108)(hereinafter "Bouquet") in view of Kim et al. (1995, Oncogene 20: 2671-2682)(hereinafter "Kim"), and further in view of Pau et al., (U.S. Patent 7,192,759)(hereinafter "Pau"), as evidenced by Bagchi et al., (Cell 1991, pp. 1063-1072)(hereinafter "Bagchi") and Renee et al., (1992, Nature pp. 82-85)(hereinafter "Renee"). Applicants respectfully disagree with this rejection.

The Action acknowledges that Bouquet does not particularly teach an immortalizing viral oncoprotein mediating disruption of complexes between avian retinoblastoma protein (Rb) and E2F transcription factors. However, the Action asserts that it was known in the art at the time the invention was made that the adenoviral E1A disrupts RB/E2F complexes (Bagchi) and that E1B 55K binds and inactivates p53 contributing to transformation of primary cells (Renee). Further, the Action asserts that it would have been obvious for one of ordinary skill in the art to substitute the vector expressing the SV40 protein or Bcl-2 of Bouquet for another viral oncogene mediating the disruption of complexes of p53, E2F and Rb as taught by Kim. Applicants respectfully disagree with this assertion.

Amended claim 1 is directed to an immortalized avian cell line that comprises the viral genes E1A and E1B 55K from mastadenovirus. None of Bouquet, Kim, Pau, Bagche or Renee disclose an immortalized avian cell line that comprises E1A or E1B 55K from mastadenovirus. An obviousness determination cannot stand here.

The Action acknowledges that the combined disclosure of Bouquet and Kim fails to specifically teach an adenovirus E1A gene and a E1B gene comprising

specific sequence. (Action, p.14). This is an understatement, for Bouquet and Kim are completely silent as to E1A or E1B 55K , and Kim discloses no viral genes whatsoever. While Bouquet discloses immortalization of cells using a viral protein (SV40) and a non-viral protein (Bcl-2), this disclosure of immortalizing a cell using a single viral protein cannot render obvious use of any viral protein to immortalize any cells, particularly cells of other species, such as avian.

The Action asserts that Pau teaches immortalization of human embryonic retina cells using E1A and E1B coding sequences. However, the immortalized cell line of Pau differs from the immortalized cell line according to amended claim 1 in that it is a **human** cell line (human embryonic retinoblast cell line PER.C6) Amended claims 1-6, however recite an immortalized **avian** cell line. Pau is silent as to the effect of E1A and E1B in avian cells. Indeed, Pau does not suggest the use of any another cell than the human embryonic retinoblast cell.

The Action asserts that one of skill in the art would have recognized that E1A and E1B would have yielded the predictable results of inducing avian cell immortalization by disrupting Rb/E2F complexes and inactivating p53, as these interactions are taught in Bagchi and Renee. Applicants respectfully disagree the Action's assertion. Pau, Bagchi, and Renee all present E1A and E1B in human or mammalian (rat baby kidney) cells. One of ordinary skill in the art would **not** expect all adenoviral proteins to function identically in avian cells as in human or mammalian cells.

One of skill in the art would not expect mastadenovirus viral proteins E1A and E1B to successfully immortalize avian cells. Human adenoviruses, such as mastadenoviruses, exist only in mammals, and have been shown to be unable to replicate in avian cells, as described in the attached "Declaration Under 37 C.F.R. § 1.132" (hereafter "Jordan Dec.") (Jordan Dec., ¶ 5) The mechanism of this discrepancy is not known, but the avian cell is unable to support this viral

regulatory pathway, which includes E1A and E1B. (Jordan Dec., ¶ 5) This would lead one of ordinary skill in the art to expect E1A and E1B to fail to perform their function effectively in avian cells.

Without some conserved protein sequence, one of skill in the art could not predict the binding activity of E1A and E1B with avian proteins merely from human or mammalian results. (Jordan Dec., ¶ 7). Indeed, the critical avian proteins in the immortalization process, such as p53, are not highly conserved between humans and birds. (Jordan Dec., ¶ 6). Upon aligning the amino acid sequences of human and chicken p53, for example, it is clear that the p53 homologs share very few conserved amino acid sequences. (Jordan Dec., ¶ 6). The binding properties of two proteins is not predictable to one of ordinary skill in the art without significant shared protein identity. (Jordan Dec., ¶ 7-8) Indeed, proteins with nearly identical amino acid sequences can display different activities in different cell types. The ability of the mastadenovirus E1A and E1B viral proteins to interact with avian E2F, and p53 in avian cells could not be predicted, and based on the lack of mastadenovirus replication in avian cells, was unexpected. (Jordan Dec., ¶ 4-8).

None of the combined references provides any teaching, suggestion, or motivation to arrive at the subject-matter of amended claim 1. Further, the lack of homology between the avian and human proteins would suggest to one of ordinary skill in the art that the E1A and E1B proteins from mastadenovirus would not function in avian cells. As such, claim 1 cannot be found obvious. Claims 2 to 7 by directly or indirectly referring to the subject-matter of claim 1 incorporate the same features that render the subject-matter of claim 1 non-obvious. Thus, also claims 2 to 7 are directed at non-obvious subject-matter.

VII. CONCLUSION

Applicants respectfully request consideration of the remarks herein. If the Examiner has any questions regarding this response, she is invited to call the undersigned attorney.

General Authorization Regarding Fees

While Applicants do not believe there are any fees due at this time, the Office is authorized to deduct any fee associated with the filing of this paper, or for any other matter related to the application, or credit any overpayment, to Deposit Account No. 13-2490.

Respectfully submitted,

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